

Res. CTPTO 14 OCT 2004

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
23 October 2003 (23.10.2003)

PCT

(10) International Publication Number  
**WO 2003/087403 A3**

- (51) International Patent Classification<sup>7</sup>: **C12Q 1/68**, G01N 33/53, A01K 67/027, A61P 25/00
- (21) International Application Number: PCT/EP2003/003958
- (22) International Filing Date: 16 April 2003 (16.04.2003)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
02008553.6 16 April 2002 (16.04.2002) EP  
60/372,424 16 April 2002 (16.04.2002) US
- (71) Applicant (for all designated States except US): **EVOTEC NEUROSCIENCES GMBH** [DE/DE]; Schnackenburgallee 114, 22525 Hamburg (DE).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **VON DER KAMMER, Heinz** [DE/DE]; Verbindungsstr. 6d, 22607 Hamburg (DE). **POHLNER, Johannes** [DE/DE]; Quittenweg 11, 22175 Hamburg (DE).
- (74) Agents: **MEYERS, Hans-Wilhelm et al.**; Postfach 10 22 41, 50462 Köln (DE).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:  
— with international search report
- (88) Date of publication of the international search report:  
21 May 2004
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: DIAGNOSTIC AND THERAPEUTIC USE OF A GOLGI PROTEIN FOR NEURODEGENERATIVE DISEASES

(57) Abstract: The present invention discloses the differential expression of golgin-245 in specific brain regions of Alzheimer's disease patients. Based on this finding, this invention provides a method for diagnosing or prognosticating a neurodegenerative disease, in particular Alzheimer's disease, in a subject, or for determining whether a subject is at increased risk of developing such a disease. Furthermore, this invention provides therapeutic and prophylactic methods for treating or preventing Alzheimer's disease and related neurodegenerative disorders using a gene coding for golgin-245. A method of screening for modulating agents of neurodegenerative diseases is also disclosed.

WO 2003/087403 A3

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/EP 03/03958

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 C12Q1/68 G01N33/53 A01K67/027 A61P25/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)  
EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE, MEDLINE, Sequence Search, EMBL

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE GENESEQ [Online] EBI; 2 July 1999 (1999-07-02), "GASTRIC CANCER ASSOCIATED GENE" XP002257871 Database accession no. AAX39745 abstract	8,11,18, 19
A	-& WO 99/04265 A (SAHIN UGUR ;TURECI OZLEM (DE); PFREUNDSCHUH MICHAEL (DE); GOUT IVA) 28 January 1999 (1999-01-28) See page 19, page 27 line 27-line 29. ----- -/--	1-7, 13-15,20

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

28 October 2003

Date of mailing of the international search report

14 01 2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Hagenmaier, S

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/03958

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FRITZLER ET AL: "MOLECULAR CHARACTERIZATION OF GOLGIN-245, A NOVEL GOLGI COMPLEX PROTEIN CONTAINING A GRANIN SIGNATURE" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, US, vol. 270, no. 52, 29 December 1995 (1995-12-29), pages 31262-31268, XP002136607 ISSN: 0021-9258	8,18,19
A	the whole document	1-7, 11-15,20
X	----- ERLICH ET AL: "MOLECULAR CHARACTERIZATION OF TRANS-GOLGI p230" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, US, vol. 271, no. 14, 5 April 1996 (1996-04-05), pages 8328-8337, XP002136608 ISSN: 0021-9258	8,18,19
A	the whole document	1-7, 11-15,20
X	----- DATABASE SWALL [Online] EBI; 16 October 2001 (2001-10-16), "GOLGI-AUTOANTIGEN" XP002256502 Database accession no. Q13439	8,18,19
A	abstract	1-7, 11-15,20
A	----- WO 00/65340 A (MYRIAD GENETICS INC) 2 November 2000 (2000-11-02) the whole document	1-8, 11-15,20
A	----- EP 1 188 839 A (EVOTEC NEUROSCIENCES GMBH) 20 March 2002 (2002-03-20) the whole document	1-8, 11-15,20
A	----- WO 02/16636 A (EVOTEC NEUROSCIENCES GMBH ;HIPFEL RAINER (DE); KRAPPA RALF (DE); P) 28 February 2002 (2002-02-28) the whole document	1-8, 11-15,20
A	----- LORING, J F ET AL: "A gene expression profile of Alzheimer's disease." DNA AND CELL BIOLOGY. UNITED STATES NOV 2001, vol. 20, no. 11, November 2001 (2001-11), pages 683-695, XP002233087 ISSN: 1044-5498	1-8, 11-15,20
	the whole document ----- -/--	

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/03958

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>PASINETTI G M: "Use of cDNA microarray in the search for molecular markers involved in the onset of Alzheimer's disease dementia." JOURNAL OF NEUROSCIENCE RESEARCH. UNITED STATES 15 SEP 2001, vol. 65, no. 6, 15 September 2001 (2001-09-15), pages 471-476, XP002233371 ISSN: 0360-4012 the whole document</p>	1-8, 11-15,20
A	<p>----- "Consensus report of the Working Group on: "Molecular and Biochemical Markers of Alzheimer's Disease". The Ronald and Nancy Reagan Research Institute of the Alzheimer's Association and the National Institute on Aging Working Group." NEUROBIOLOGY OF AGING. UNITED STATES 1998 MAR-APR, vol. 19, no. 2, March 1998 (1998-03), pages 109-116, XP002233088 ISSN: 0197-4580 the whole document</p>	1-8, 11-15,20
T	<p>----- WO 02/38803 A (DEUTSCHES KREBSFORSCH ;USENER DIRK (DE); EICHMUELLER STEFAN (DE);) 16 May 2002 (2002-05-16) the whole document</p> <p>-----</p>	1-8, 11-15,20

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/EP 03/03958

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 9  
because they relate to subject matter not required to be searched by this Authority, namely:  
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy
2. ☒ Claims Nos.: 10  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☒ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:  
1-15, 18-20 (completely)
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-15,18-20 (completely)

Methods of diagnosing, prognosticating, monitoring the progression or evaluating a treatment of a neurodegenerative disease comprising determining the level and/or activity of a transcription/translation product of a gene coding for golgin 245 in a sample as well as a kit for diagnosing or prognosticating a neurodegenerative disease comprising at least one reagent that selectively detects a transcription/translation product of a gene coding for golgin 245, a protein molecule being a translation product of the gene coding for golgin-245 for use as a diagnostic /screening target for a neurodegenerative disease, use of an antibody specifically immunoreactive with an immunogen, wherein said immunogen is a translation product of a gene coding for golgin-245 for detecting a neurodegenerative disease; a recombinant, non-human animal comprising a non-native gene sequence coding for golgin-245; assays or method for screening for a modulator of neurodegenerative diseases of one or more substances selected from the group consisting of the golgin 245 gene, the transcription or translation product of said gene.

---

2. claims: 16,17 (completely)

An assay for testing a compound, preferably for screening a plurality of compounds for inhibition of binding between a ligand and golgin-245 protein and an assay for testing a compound, preferably for screening a plurality of compounds to determine the degree of binding of said compounds to golgin-245 protein.

---

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Claims Nos.: 9

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

-----

Continuation of Box I.2

Claims Nos.: 10

Present claim 10 relates to a product defined by reference to a desirable characteristic or property, namely being a modulator of an activity or a level of at least one substance selected from the group listed in claim 10 under (i)-(iv). The claim covers all products having this characteristic or property, whereas the application does not provide any support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for such products. In the present case, the claim so lacks support, and the application so lacks disclosure, that a meaningful search is impossible. Independent of the above reasoning, the claim also lacks clarity (Article 6 PCT). An attempt is made to define the product by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search impossible. Consequently, no search has been carried out for claim 10.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 03/03958

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9904265	A	28-01-1999	US 6218521 B1	17-04-2001
			US 6043084 A	28-03-2000
			US 6403373 B1	11-06-2002
			AU 8571598 A	10-02-1999
			EP 0996857 A2	03-05-2000
			JP 2001516009 T	25-09-2001
			WO 9904265 A2	28-01-1999
			US 2002037541 A1	28-03-2002
			US 6517837 B1	11-02-2003
-----				
WO 0065340	A	02-11-2000	AU 4475400 A	10-11-2000
			CA 2371006 A1	02-11-2000
			EP 1181549 A1	27-02-2002
			JP 2002542774 T	17-12-2002
			WO 0065340 A1	02-11-2000
-----				
EP 1188839	A	20-03-2002	EP 1188839 A1	20-03-2002
-----				
WO 0216636	A	28-02-2002	AU 8983401 A	04-03-2002
			WO 0216636 A2	28-02-2002
			EP 1377678 A2	07-01-2004
-----				
WO 0238803	A	16-05-2002	DE 10055285 A1	06-06-2002
			AU 1897702 A	21-05-2002
			WO 0238803 A2	16-05-2002
			EP 1349871 A2	08-10-2003
-----				